

WHAT IS CLAIMED IS:

- 1 1. A method for producing a non-human animal model of a human or non-human
2 animal disease which comprises transferring at least one aberrant form of at least one
3 gene known to be associated with said disease in humans or non-human animals into
4 appropriate tissue of a living non-human animal under conditions which result in the
5 expression of said at least one aberrant gene, wherein said transferring does not require
6 the modification of the germ-line of said living animal.
- 1 2. The method according to claim 1 wherein said human or non-human animal
2 disease is a neurodegenerative disease.
- 1 3. The method according to claim 2 wherein said human disease is selected from the
2 group consisting of Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease.
- 1 4. The method according to claim 3 wherein said at least one gene is an aberrant
2 form of tau. B
- 1 5. The method according to claim 3 wherein said aberrant form of tau is P301L,
2 associated with "fronto-temporal dementia with Parkinson's linked to chromosome 17
3 (FTDP-17)".
- 1 6. The method according to claim 3 wherein said at least one gene is an aberrant
2 form of alpha-synuclein.
- 1 7. The method according to claim 6 wherein said aberrant form of alpha-synuclein is
2 mutant α -synuclein (A30P), associated with Parkinson's Disease.
- 1 8. The method according to claim 3 wherein said at least one gene is a mutant
2 amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or combinations thereof,
3 associated with Alzheimer's Disease.

1 9. The method according to claim 1 which comprises identifying a combination of
2 genes relevant to a particular human pathology and somatically transferring combinations
3 of said genes into tissues appropriate to said particular human pathology in a non-human
4 animal model appropriate to said human pathology.

1 10. The method according to claim 1 comprising:

- 2 (a) controlling the location to which the genes are transferred, that is spatially
3 controlling gene expression of the transferred genes, in the non-human animal
4 model to which said at least one gene is transferred;
- 5 (b) controlling the temporal effects of transferred genes at specific times in the
6 development of otherwise normal organisms, or in the development of organisms
7 in which germline modifications have previously been made, by selecting the time
8 at which said transferred genes are introduced into said organism, or by
9 controlling the time of expression of said transferred genes;
- 10 (c) evaluating the effects of expression of combinations of multiple transgenes, which
11 in a germline transgenic non-human animal would be difficult if not impossible to
12 achieve due to diseases which might prevent the animal model from maturing to
13 the age-appropriate state for modeling onset of a particular, complex human
14 disease;
- 15 (d) increasing the rate for analyzing multiple genes which contribute to complex,
16 multifactorial human diseases by transferring more than a single gene into an
17 appropriate non-human animal model for said disease;
- 18 (e) testing pharmaceutical agents for their ability to ameliorate specific diseases
19 induced in said non-human animal model;
- 20 (f) studying specific human pathologies induced in said non-human animal model by
21 inducing said pathology in said animal model by transferring said at least one
22 gene into said animal model;
- 23 (g) supplementing an existing germline transgenic model with additional somatically
24 provided gene products to modulate the transgenic model;
- 25 (h) creating a disease condition in an otherwise healthy animal; and
26 (i) combinations of (a) –(h).

1 11. A non-human animal produced by the method of claim 1.

1 12. A pharmaceutical identified through testing of pharmaceutical compounds
2 using the non-human animal produced according to claim 11.

1 13. A method for inducing neurofibrillary tangles in the brain of a non-human
2 animal which comprises injecting into the brain of said animal an effective amount of
3 a gene expression construct encoding tau, alpha-synuclein, presenilin-1, amyloid
4 precursor protein, IL6, or a combination thereof.

1 14. A non-human animal produced according to the method of claim 13.

1 15. A method for inducing behavioral changes in a non-human animal model
2 which comprises somatic administration of at least one gene directly to the brain of
3 said non-human animal, wherein said at least one gene is associated with a human
4 neurodegenerative disease. B

1 16. The method according to claim 1 wherein said at least one aberrant form
2 of said at least one gene is transferred by means of an adeno-associated virus.

1 17. A composition comprising at least one gene construct adapted for
2 producing a non-human animal model of a human or non-human-animal disease by
3 transferring at least one aberrant form of at least one gene known to be associated
4 with said disease in humans or non-human animals into appropriate tissue of a living
5 non-human animal under conditions which result in the expression of said at least one
6 aberrant gene, wherein said transferring does not require the modification of the
7 germ-line of said living animal, said composition comprising said at least one
8 aberrant gene in a vector construct which results in active expression of said gene
9 upon introduction into said tissue.

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1 18. The composition according to claim 17 wherein said at least one gene is
2 an aberrant form of tau.

1 19. The composition according to claim 18 wherein said aberrant form of tau
2 is P301L, associated with "fronto-temporal dementia with Parkinson's linked to
3 chromosome 17 (FTDP-17)".

1 20. The composition according to claim 17 wherein said at least one gene is
2 an aberrant form of alpha-synuclein.

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1 21. . The composition according to claim 20 wherein said aberrant form of
2 alpha-synuclein is mutant α -synuclein (A30P), associated with Parkinson's Disease.

1 22. . The composition according to claim 17 wherein said at least one gene is a
2 mutant amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or
3 combinations thereof, associated with Alzheimer's Disease.

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